Targeted enrichment with Watchmaker TAPS+ distinguishes immune cell types by methylation signal in concordance with WGS

Can Kockan, Carrie Cibulskis, Michelle Cipicchio, Fabiana Duarte, Mark Fleharty, Chris Kachulis, Sophie Low, Sam Pollock, Micah Rickles-Young, Indranil Singh, Ruochi Zhang, Jason Buenrostro, Sean Hofherr, Niall Lennon

Introduction

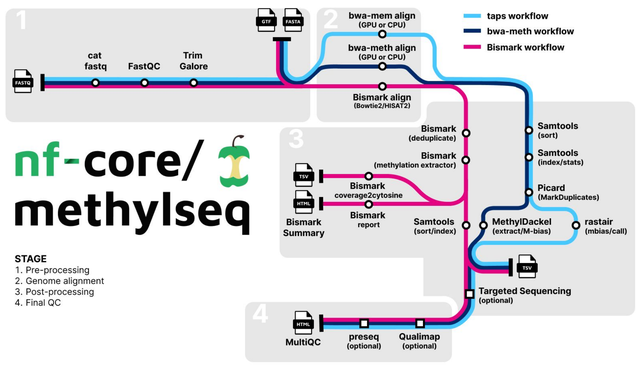
TAPS+ is a new technology offered by Watchmaker Genomics that achieves methylation signal detection through converting only the methylated C's in the genome to T's as opposed to bisulfite sequencing methods. We performed a series of experiments with TAPS+ to evaluate its applicability in different scenarios.

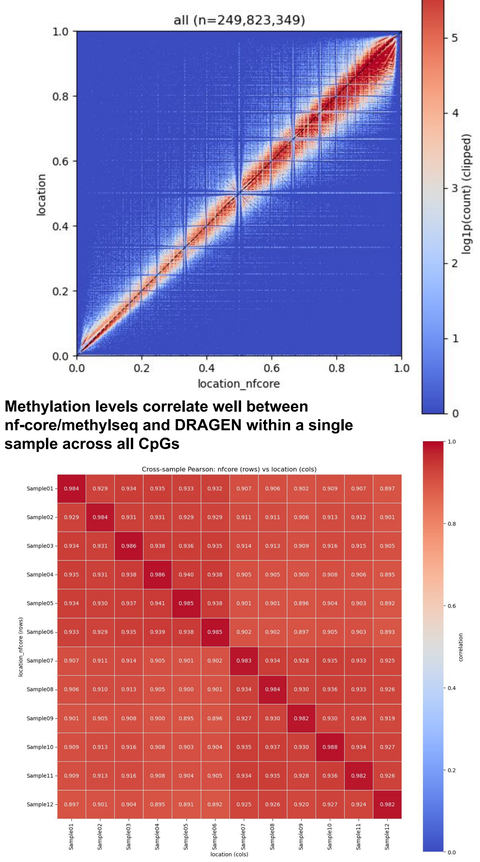
Data

Sample Type	Sequencing Method	# Samples
Cell-Line	WGS	12
Immune Cells	WGS	11
Immune Cells	Targeted (Enrichment)	11
cfDNA	WGS	18
Mouse	WGS	12

TAPS+ Allows Flexible Use of Computational Pipeline(s)

TAPS+ data in the form of fastq files can be processed multiple ways. The nf-core/methylseq pipeline describes the basic steps of required analysis. Due to advantages in processing speed we used Illumina DRAGEN which includes TAPS support, but we show that these pipelines agree well with each other using the set of mouse samples.

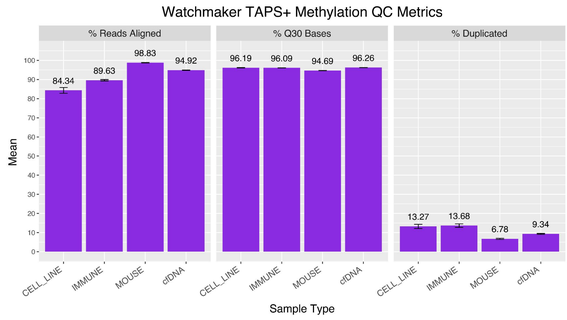


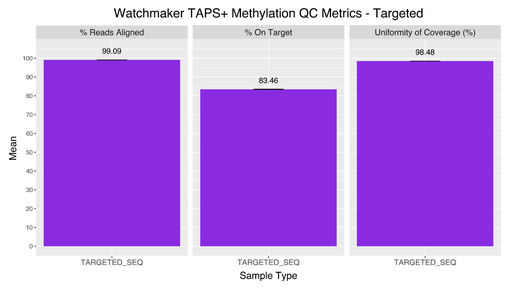


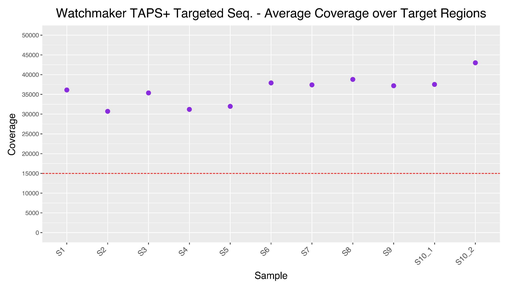
Methylation levels correlate well between nf-core/methylseq and DRAGEN within a single sample across all CpGs

Pairwise overall methylation levels across the 12 mouse samples also correlate well between nf-core and DRAGEN

TAPS+ QC Metrics Across Different Sample Types - WGS and Targeted

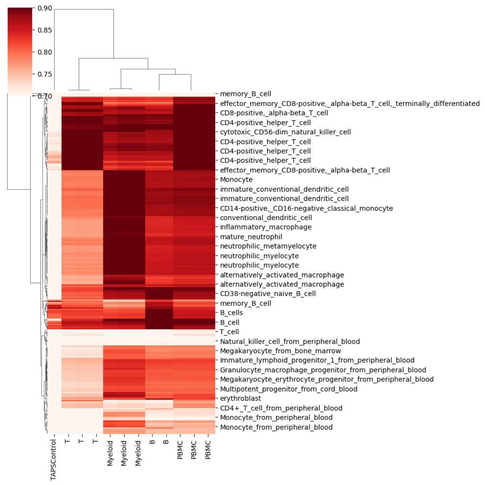




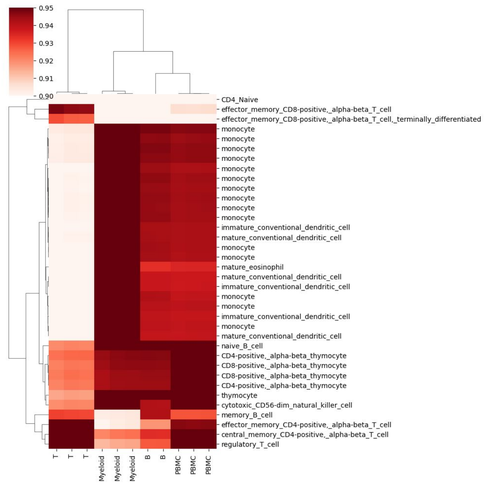


TAPS+ Methylation Signal Allows Distinguishing Immune Cell Types

TAPS+ QC - ATAC-seq peaks - WGS



TAPS+ QC - ATAC-seq peaks - Targeted - Promoter Panel

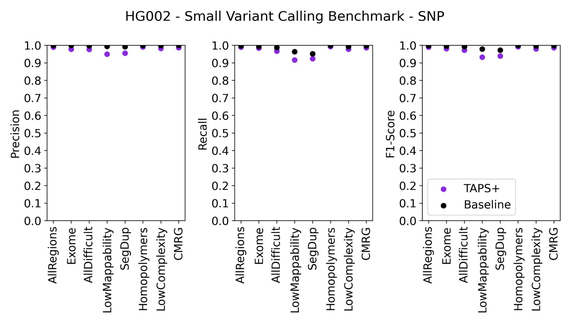


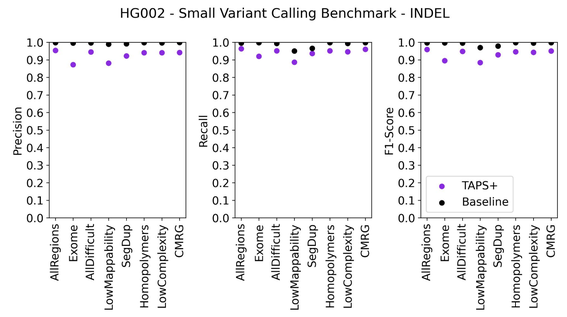
Findings from our initial experiments suggest a targeted assay to deconvolve cell types from blood & measure environmental exposures is possible (and scalable to large biobanks with TAPS+)

TAPS+ Allows Detection of Structural Variants Due to Improved Alignment

IGV visualization of methylation sequencing data from cell-line A673 showing clear evidence of the expected gene fusion event. TAPS+ enables high quality alignment needed to detect fusion breakpoints.

TAPS+ Enables Standard WGS Level Small Variant Calling Along with Methylation Signal





Conclusions

Through a series of experiments we found that TAPS+ provides a promising solution for:

- Whole Genome Methylation Profiling
- Targeted Panel Methylation Profiling
- Small Variant Calling as well as SV Calling

Subsequently we were successfully able to classify immune cells based on their methylation profile for both WGS and targeted sequencing approaches, ***even when a promoter panel not ideal for the task was used***.

References

1. https://www.watchmakergenomics.com/media/wg/asset/%2Fm%2F4%2Fm417_taps_data_analysis_tn_wmtn003_v1-0-1125.pdf
2. https://github.com/nf-core/methylseq

Contact

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Broad Clinical Labs
genomics@broadinstitute.org

Can Kockan
kockan@broadinstitute.org